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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/853,457	05/10/2001	David P. Dumas	P-PR 4674	6690

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EXAMINER	
LIU, SUE XU	

ART UNIT	PAPER NUMBER
1639	

DATE MAILED: 07/08/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/853,457	DUMAS, DAVID P.	
	Examiner	Art Unit	
	Sue Liu	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04/18/2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-47* is/are pending in the application.

4a) Of the above claim(s) *1-11, 17, 18, 22-37, and 43-44* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *12-16, 19-21, 38-42, and 45-47* is/are rejected.

7)☒ Claim(s) *12* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *10 May 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *08/06/01; 09/03/02*. 02/25/03
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of a method of determining an epitope in a sample (inventions of Group III) in the reply filed on 10/12/2004 is acknowledged. The traversal is in respect to the division of the claims of Group III from the claims of Group II. The applicant's argument is based on the ground that a thorough search of the claims of either group will likely reveal art relevant to the examination of the claims of the other group. This argument is not found persuasive, because 1.) The invention of Group II composition (comprises of reagent ligands and reagent antibodies) is different from the composition used in Group III method, which comprises three components: reagent ligands, reagent antibodies and a sample; 2.) The composition of Group II can be used in a materially different process from Group III. For examples, the Group II composition can be used for antibody purification and immunoassays. Thus, restriction is proper, and Claims 7-11 of Group II are withdrawn.

The requirement is still deemed proper and is therefore made FINAL.

2. Claims 7-11 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention of a composition, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 10/12/2004.

3. Applicant's non-election of inventions of Groups I, IV, V and VI without traverse in the reply filed on 10/12/2004 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 1-6 and 22-37 of Groups I, IV, V and VI are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected inventions of compositions and methods, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 10/12/2004.

4. Applicant elected without traverse of the following species, "peptide as the species of the ligand," and "organism as the species of sample." In Claims 16 and 42, "a cell," "a tissue," and " a body fluid" are withdrawn due to non-elected species. Claims 17, 18, 43 and 44 are withdrawn due to non-elected species. In Claims 8, 15, and 41, "oligosaccharides," "oligonucleotides" and "organic molecules" are withdrawn due to non-elected species.

5. Claims 1-47 are currently pending;

Claims 1-11, 17, 18, 22-37, and 43-44 have been withdrawn;

Claims 12-16, 19-21, 38-42, and 45-47 are being examined in this application.

Priority

6. This application claims priority to provisional application 60/325,766 filed on 05/12/2000.

Specification

7. The disclosure is objected to because of the following informalities: The Provisional application serial number is incomplete. See Page 1, line 5 of the Specification.

Appropriate correction is required.

Claim Objections

8. Claim 12 is objected as being dependent on non-elected Claim 7. Applicant is requested to amend Claim 12 to include all the limitations of Claim 7.

Claim Rejections - 35 USC § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10. Claims 12-16, 19-20, 38-42, 45, and 46 are rejected under 35 U.S.C. 102(b) as being anticipated by Savoca et al (*Journal of Immunological Methods* 1991; 141: 245-252). The reference was provided by applicant in PTO 1449, filed on 8/06/2001.

The instant claims briefly recite a method for determining epitope in a sample by contacting the sample with a population of reagent ligands attached to solid support in an array and a population of reagent antibodies. In the presence of competing epitope(s) in a given sample, the reagent antibodies specifically bind to a subset of reagent ligands, and leave a

portion of the reagent ligands unbound. The reagent antibodies that are unbound to the reagent ligands have specificity for the competing epitopes present in the given sample. The binding interactions between reagent antibodies and reagent ligands are indicated by labels attached to the reagent antibodies, and thus allow the detection of epitopes in a sample by determining the identity of the unbound reagent ligands in the array.

Savoca et al teach a method of epitope mapping employing immobilized synthetic peptides. The reference teaches synthesis of pin bound peptides with various amino acid sequences by using the epitope mapping kit from Cambridge Research Biochemicals. (See Material and Methods section in the reference.) This reads on the limitations of "a diverse population of reagent ligands attached to a solid support" of the instant claims. This would also read on the limitation that the "said reagent ligands are on an array" (see the instant Claims 19, and 45).

The reference teaches usage of antisera raised against a protein. It is well known in the art that antiserum contains polyclonal antibodies, which constitute a diverse population of antibodies. This refers to the limitation of a "diverse population of reagent antibodies" and "a diverse population of reagent binding molecules." (See the instant Claims 12 and 38.)

The reference teaches binding of the antisera to the pin bound peptides in a competitive ELISA assay. The competitors in the ELISA assay are proteins (e.g. cytochrome c) and free peptides. (See the Material and methods section of the reference.) These competing proteins (sections of an organism) and free peptides constitute samples, thus read on the limitation of "a sample" recited in the instant claims.

The reference teaches the specificity of the reaction between anti-cytochrome c antibodies (IgG) and pin-bound hexapeptides of cytochrome c was tested using a competitive ELISA in which proteins or free peptides and pin-bound peptides competed for the antibody. The references further teaches "competition was specific for many of the pin-bound peptides." (See Abstract and Results of the reference.) This reads on steps (a) and (b) of the instant Claims 12 and 38, as well as limitations recited in the instant Claims 13, 14, 39, and 40.

The reference teaches the antibodies are labeled with a secondary antibody. (See the Materials and Methods section of the reference.) This reads on the limitation of "said reagent binding molecules are labeled" as directed in the instant claims. Thus, the reference clearly anticipates the claimed invention.

11. Claims 12-16, 19-20, 38-42, 45, and 46 are rejected under 35 U.S.C. 102(b) as being anticipated by US Patent 5,595,915 (Geysen et al).

Geysen teaches a method of detecting or determining amino acid sequence, which is antigenically active. The method comprises the steps of synthesizing a plurality of peptides, contacting the peptides with antibodies, and detecting specific antibody-antigen interactions. The reference specific teaches "synthesizing a plurality of peptides, wherein each of said peptides is coupled to a solid phase and said plurality of peptides is arranged in an array..." (See Column 8 lines 5-10 (Claim 1) of the reference.) This directly anticipates the limitation of "A diverse population of reagent ligands attached to a solid support."

Geysen teaches "contacting said array of said peptides with antibody against the protein or portion thereof..." as directed in the Claims 1 and 2 of the reference. The reference also

teaches the preparation of various antisera against virus particles or portions thereof. Geysen further teaches using the said antisera enzyme-linked immunosorbent assay with a peptide library. (See Examples 1-3 of the references, e.g. lines 25-67 of Column 5.) As it is well known in the art, antisera contain diverse population of antibodies. Therefore, the reference reads on the limitation of "composition comprising...a diverse population of reagent antibodies" or " a diverse population of reagent binding molecules."

The reference teaches the detection of the interactions between the peptides and the antibodies by using indirect ELISA assay, where the antibodies are labeled by conjugated secondary antibodies. (See Examples 1-3 of the reference.) The reference teaches a portion of the antibodies specifically bind to a subset of the peptide library as indicated by the generated "antigenic profiles," which indicates both bound and unbound peptides.

The reference teaches detection of antibody-antigen complex formation after exposure to complete virus particles. (See lines 30-35 from Column 5, lines 1-5 of Column 7, and lines 40-45 Column 7 in the reference.) The purified complete virus particles constitute as a sample. The reference teaches the population of antibodies contained in the antisera specifically bind to the library of peptides or a portion thereof. The reference also teaches the said population of antibodies contained in the antisera specifically bind to virus particles (which constitute organisms) presented in a sample. (See Example 1.) The reference further teaches a method comprising the peptide library, the antibodies and the complete virus particles in a binding assay.

Therefore, the reference anticipates the instant Claims 12-16, 19-20, 38-42, 45, and 46 by directing a method of generating "antigenic profiles" using a peptide array, a diverse

population of antibodies (polyclonal antibodies), and a sample containing specific competitive antigens (the whole virus particles).

Claim Rejections - 35 USC § 103

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

13. Claims 12-16, 19-21, 38-42, and 45-47 are rejected under 35 U.S.C. 103(a) as being obvious over Metzler et al (*Arteriosclersosis, Thrombosis, and Vascular Biology* 1997; 17: 536-541), and Schell et al (Journal of Cancer Research and Clinical Oncology. 1993; 119:221-226.)

The instant claims briefly recite a method for determining epitope in a sample by contacting the sample with a population of reagent ligands attached to solid support in an array and a population of reagent antibodies. In the presence of competing epitope(s) in a given sample, the reagent antibodies specifically bind to a subset of reagent ligands, and leave a portion of the reagent ligands unbound. The reagent antibodies that are unbound to the reagent ligands have specificity for the competing epitopes present in the given sample. The binding interactions between reagent antibodies and reagent ligands are indicated by labels attached to the reagent antibodies, and thus allow the detection of epitopes in a sample by determining the identity of the unbound reagent ligands in the array. The detection label is specifically a fluorescent label.

Metzler et al teach epitope mapping of an antigen by using a library of peptides generated on solid support. The references teach the generation of antisera containing a population of antibodies against a specific antigen. Competitive ELISA assays are also taught by the references employing samples containing the specific antigens, the antibodies and peptide library.

Metzler et al teach the synthesis of peptide library on solid support. For example, Metzler et al teach the generation of 526 of "7-mer peptides" on polyethylene pins using an epitope scanning kit. (See "Pin ELISA" under the Methods section of the reference.)

Metzler et al teach the usage of antisera containing polyclonal antibodies. For example, Metzler et al teach a population of anti-hsp65/60 antibodies from pooled human sera obtained from subjects aged 65 and older. (See " Serum Samples and Ab Determination" and "Affinity Chromatography of Anti-hsp65/60 Ab" under the Methods section of the reference.)

Metzler et al teach the detection of the binding activity of the antibodies and the peptides. For example, Metzler et al teach using ELISA assay to measure antibody binding to the peptide library. (See "Pin ELISA" under the Methods and the Results sections of the reference.)

Metzler et al teach the detection of a binding molecule in a sample with the peptide library and the population of antibodies. Specifically, Metzler et al teach "comparing peptide binding of anti-hsp65/60 Ab in the presence or absence of blocking by 50-fold excess recombinant hsp65." (See "Pin ELISA" under the Methods and the Results sections of the reference.) Specific binding activity of the anti-hsp65/60 antibodies to recombinant hsp65 is demonstrated by Western Blotting and competitive ELISA assays. For example, in the presence of the recombinant hsp65, the reference teaches that there is a portion of the peptides that are unbound by the antibodies. (See "Western Blotting" and "Pin ELISA" under the Results section.)

Metzler et al teach a detection method through the labeling of antibodies. For example, Metzler et al teach using an HRP-goat anti-human secondary antibody conjugate to detect antibody and peptide binding. (See "Pin ELISA" under the Methods section.) The HRP-goat anti-human secondary antibody specifically binds to or labels the human antibodies. Through the addition of substrate, the human antibodies are labeled and detected.

Metzler et al teach the usage of a colorimetric label to detect antibodies binding to ligands. The reference does not teach a fluorescent label for the used antibodies. Schell et al teach competitive ELISA assays conducted using both colorimetric and fluorescent labels. It was demonstrated by the reference that the fluorescent label provides lower detection limit than the colorimetric labels, hence provides more sensitive detection results. Schell et al teach the advantage of using a fluorescent label instead of a colorimetric label. Therefore, it would have been obvious for one of ordinary skill in the art at the time of the invention was made to replace the colorimetric label to a fluorescent label for the antibody. In addition, it is well know in the art that various labels such as colorimetric, fluorescent, and radioactive labels can be used in detecting antibody-antigen complexes. A person skilled in the art at the time of the invention was made would have been motivated to use fluorescent labels, because fluorometer for signal detection as well as fluorescent based immunoassay kits were readily available at the time of the invention, and would have provided a convenient alternative to colorimetric detection.

Conclusion

No Claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sue Liu whose telephone number is 571-272-5539. The examiner can normally be reached on M-F 9am-3pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Sue Liu
Art Unit 1639
6/28/2005

PADMASHRI PONNALURI
PRIMARY EXAMINER